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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/724,900	12/02/2003	J. Glenn Morris	62610.000035	2442

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EXAMINER	
JOIKE, MICHELE K	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 11/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/724,900	MORRIS ET AL.	
	Examiner	Art Unit	
	Michele K. Joike, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *18-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/07/04, 09/26/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on September 21, 2006 is acknowledged. The traversal is on the ground(s) that searching all of the inventions together, particularly Groups I and II would not constitute an undue search burden. This is not found persuasive because the methods in Groups I and II present different steps. For example, one of the methods of Group II comprises applying a bacteriophage preparation to medical equipment to reduce the incidence of VRE infection; the steps in the method of Group I comprise treating a patient with a pharmaceutical composition containing bacteriophage. Group III claims a bacteriophage, which could be used in other methods than the ones outlined above. The searches are different and would present an undue burden.

Claims 18-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventins, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on September 21, 2006.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-17 are examined.

Specification

The disclosure is objected to because of the following informalities: There are a number of spelling and grammatical errors. Specifically, p. 5, line 8,

"emerge" should be "emergence"; p. 6, lines 8-17 are underlined for no apparent reason; p. 10, line 14, a range between 8095% is recited; p. 18, line 23 "mariner" should be "manner"; p. 21, line 19, "page" should be "phage"; p. 22, line 6, "ors" should be "on"; p. 23, line 21, "tire" should be "the"; and on p. 33, line 29, "charity" should be "clarity".

Appropriate correction is required.

Claim Objections

Claim 6 is objected to because of the following informalities: It appears that "MDSA" should be "MDRSA". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13 – 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 13 recites the language "the selected bacteria who are admitted to said medical facility." The phrase "who are admitted to said medical facility" is a misplaced modifier.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make

and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims any lytic bacteriophage and methods of using the bacteriophage to reduce the risk of bacterial infection or sepsis in a susceptible patient by treating the patient with a pharmaceutical composition containing the bacteriophage, and to reduce the risk of incidence of infection by reducing colonization of bacteria after a bacteriophage preparation is administered. The claims read on a broad genus of bacteriophage (and compositions thereof) comprising bacteriophage that have the ability to reduce the risk and incidence of infection by a broad genus of bacteria.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show applicants were in possession of the claimed genus. In the instant case, the specification does not sufficiently describe a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics.

Applicant claims a bacteriophage and method of using the bacteriophage to reduce the risk and incidence of infection in a medical facility by function only, without any disclosed or known correlation between the elements and their function. The specification only provides teachings regarding the identification of seven particular bacteriophage with the ability to infect a range of VRE in a culture environment, two of which are specifically stated as having a narrow range of VRE specificity (VRE/E2 and VRE/E3; see for example page 30, lines 15-18) and therefore do not themselves meet the limitations of infecting such a broad range of VRE. The specification also does not teach what features of the phage are required to lytically infect a broad genus of bacterial strains and theoretically confer the ability to reduce the incidence of bacterial infection in a medical facility, therefore the skilled artisan cannot envision a sufficient number of phage or phage preparations to describe the claimed genus. The skilled artisan cannot envision a sufficient number of embodiments of the instant invention from the instant specification because the specification only discloses seven particular phages, two of which have a much narrower range of specificity than that which is claimed in preferred embodiments of the claims, without a description of a structure-function relationship as it concerns the ability of the phage to lytically infect of broad range of VRE and to reduce the incidence of VRE infection in a medical facility. Furthermore, none of the seven isolated phage are further characterized in a way that might provide a basis for the skilled artisan to envision additional phage capable of satisfying the functional limitations of the claims. Because the skilled artisan cannot envision any other phage or

phage preparations that would have the claimed function, the skilled artisan would not be apprised that the applicant was in possession of the claimed genus, nor would the skilled artisan be able to envision what other bacteriophage could be used in the claimed method and have the required function of reducing the incidence and risk of bacterial infection in a medical facility.

The prior art does not provide sufficient information on the subject to overcome the deficiencies of the instant specification. There is no description in the prior art of phage that can function to infect such a broad a range of specificity of host cells such as that claimed in the instant application. Thus the skilled artisan cannot rely on the prior art to envision a sufficient number of embodiments of the instant invention to see that the applicant was in possession of the claimed genus.

In conclusion, applicant has disclosed that they have isolated seven specific bacteriophage with the functional ability to infect a broad range of VRE in a culture environment, although two such phage are cited as having a narrow range of specificity. There is no description of the characteristics of these phage that confer virility against such a broad genus of VRE, and seven phage are not deemed a representative number to describe any phage that has the ability to infect such a broad range of VRE. These two facts, in conjunction with the fact that there is no description in the prior art of characteristics of phage that allow them to infect such a broad range of host cells, make it impossible for the skilled artisan to envision the claimed genus of bacteriophage having the functional ability to infect such a broad range of bacterial host cells. Because the skilled

artisan cannot envision the broadly claimed genus of bacteriophage and preparations thereof, the skilled artisan would reasonably conclude that applicants were not in possession of the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The nature of the invention is methods of using any lytic bacteriophage to reduce the risk of bacterial infection or sepsis in a susceptible patient by treating the patient with a pharmaceutical composition containing the bacteriophage, and to reduce the risk of incidence of infection by

reducing colonization of bacteria after a bacteriophage preparation is administered.

Breadth of the claims: The claims are extremely broad because any bacterium can be treated with any lytic bacteriophage.

Working examples and Guidance of the specification: The claims are directed to methods of reducing the risk or incidence of infection, as opposed to a method of treating, which means the claims are drawn to preventative means, and the bacteria are not prevented from infecting the host.

The specification teaches the isolation of seven particular phage, disclosed as having a broad range of host specificity to VRE (including at least three different VRE species: *E. faecium*, *E. gallinarium* and *E. faecalis*) under culture conditions. However, it is also indicated that a cocktail comprising all seven strains was only capable of lysing 95% of the 234 VRE species tested (see for example Ex. 3 on page 30 of the specification). The specification further indicates that the direct inoculation of VRE infected mice *in vivo* resulted in at least a 1 log reduction of colonization (see for example Ex. 5, page 32), but does not comment on whether the mouse was still infected. The specification then describes a hypothetical study to determine the ability of these phage to be used as a medicament for humans infected by VRE, although the description is made in the future tense and no such demonstration as to the efficacy of the treatment is made in the specification. Furthermore, there is no teaching that suggests that the phage, even when directly applied, will reduce infection by VRE, only that it reduces the colonization. Infection and colonization are distinct parameters.

Upon considering the maximum efficacy of the bacteriophage preparation disclosed in the instant specification, 5 out of every 100 strains survive. While this reduces the overall colonization in terms of the overall number of strains that are present, there is no indication that the remaining 5 strains do not have the ability to infect an individual, wherein they can cause medical problems.

Predictability and state of the art: The art is highly unpredictable on a number of levels. First, the bacteriophage must be able to remain viable in the host to which it is applied. Second, even if the phage is able to infect bacteria in the patient, the phage must also be able to maintain its effectiveness to infect the broad genus of bacteria. Finally, the phage must be able to adequately lyse the bacteria such that it reduces the incidence of infection in a medical facility.

Applicants *in vivo* mouse model, while showing a reduction in colonization of VRE, does not predictably indicate that the mice are no longer subject to infection by VRE (i.e., the reduction in colonization *in vivo* does not necessarily indicate that the infection has been cured). In Barrow et al (Clin. and Diagnostic Lab. Immun. 5(3): 294-298, 1998, specifically p. 296), chickens were inoculated with phage 1, 2, or 5 days before being injected with *E. coli*. One chicken out of seven died when given the phage prophylacticly at 1 and 2 days before *E. coli* injection. Three out of seven (43%) died when given the phage prophylacticly at 5 days. Prophylactic application did not prevent infection or even death. It did not even reduce the risk of infection, since four out of nine (44%) chickens that were not given the phage died from the *E. coli* infection. The art is silent on the ability of prophylactic application being used to prevent infection in human

patients. Furthermore, there is no indication in the specification at what point the phage needs to be applied to the patient to reduce the risk or incidence of infection. Therefore, the skilled artisan would need to practice undue and unpredictable trial and error experimentation to determine how the claimed method worked.

Amount of experimentation necessary The demonstration in the instant specification indicates that only 95% of the tested VRE strains were infected by a composition comprising all 7 of the bacteriophage that have been isolated in the instant specification. Although the rate of infection of the host cell range is very good, there are still 5% of VRE strains that remain viable and capable of causing nosocomial infection. From this data, the skilled artisan could not reasonably predict that the remaining 5% of the VRE strains would not spread in a similar manner, if not better due to the lack of a competitive selective pressure with other VRE strains, throughout the medical facility. This indeed would not reduce the incidence of VRE infection, although it could reduce the colonization of several types of VRE within the facility. Because there is no scientific data to suggest that 5% of VRE strains would be insufficient to maintain the incidence of VRE in a medical facility, one cannot reasonable predict the prophetic recitation of reduced incidence in VRE infection in a medical facility by applying a bacteriophage preparation. In order to use the claimed invention, the skilled artisan would be forced to perform undue and unpredictable trail and error experimentation to establish that the claimed reduction of VRE colonization was sufficient to reduce the overall VRE infection rate in a medical facility.

In view of the breadth of the claims and the lack of guidance provided by the specification as well as the unpredictability of the art, the skilled artisan would have required an undue amount of experimentation to make a lytic bacteriophage that could lyse any bacteria, thereby preventing infection.

Allowable Subject Matter

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele K. Joike, Ph.D. whose telephone number is 571-272-5915. The examiner can normally be reached on M-F, 9:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michele K Joike, Ph.D.
Examiner
Art Unit 1636

DAVID GUZO
PRIMARY EXAMINER